

WHAT IS CLAIMED IS:

1. A composition comprising:

- (a) a podophyllotoxin, an analog thereof or derivative thereof, and  
(b) a surfactant;

5 wherein the composition forms a micelle.

2. The composition of claim 1 wherein the podophyllotoxin derivative is etoposide or teniposide.

3. The composition of claim 1 wherein the podophyllotoxin derivative is selected from the group consisting of derivatives of podophyllotoxin modified in rings C and E including  
10 epidodophyllotoxin, deoxypodophyllotoxin,  $\beta$ -peltatin, 4'-demethylpodophyllotoxin, 4'-demethylepipodophyllotoxin, 4'-demethyldeoxypodophyllotoxin,  $\alpha$ -peltatin, VM-26 (teniposide), VP-16-213; derivatives modified in ring D including deoxypodophyllotoxin, podophyllotoxin-cyclic ether, deoxypodophyllotoxin-cyclic ether, deoxypodophyllotoxin-cyclopentane, deoxypodophyllotoxin-cyclopentanone, podophyllotoxin-cyclic sulfide,  
15 deoxypodophyllotoxin-cyclic sulfide, podophyllotoxin-cyclic sulfone, deoxypodophyllotoxin-cyclic sulfone; derivatives picropodophyllotoxin, dehydropodophyllotoxin, glucoside derivatives of VP-16 and VM-26, 4'-demethylepipodophyllotoxin and glucoside derivatives, acetal and ketal derivatives of 4'-demethylepipodophyllotoxin- $\beta$ -D-glucoside (DMEPG), epipodophyllotoxin- $\beta$ -D-glucoside (EPG); compounds with A-ring modifications: podophenazine, 2',3'-dichloropodophenazine, benzopodophenazine and their 4 $\beta$ -p-nitroaniline derivatives; compounds with B-ring  
20 modifications:  $\alpha$ -peltatin esters and ethers including its glycosidic ethylidene and thenilidene cyclic acetals; compounds with C-ring modifications: ring C aromatized analogues of podophyllotoxin, benzodioxole lactones which are analogues of podophyllotoxin, triazene and aziridine derivatives of podophyllotoxin such as 4-oxa-2-podophyllotoxin and 4-thia-2-azapodophyllotoxin; compounds with D-ring modifications: picropodophyllotoxin which is the thermodynamically stable cis epimer of podophyllotoxin, and its other cis analogues and trans isomers, the cyclopentane and cyclopentanone derivatives, the hydroxy derivatives such as anhydropodophyllol and deoxyanhydropodophyllol, the series of 2-substituted

podophyllotoxine derivatives including 2-methyl, 2-chloro-2-hydroxy- and 2-bromopodophyllotoxin, and the derivative N'-podophyllotoxin-N-[3-(2,2,5,5-tetramethylpyrrolinenyloxy)]semi-carbazide (GP-11), etoposide lactam; the desoxy E-ring analogues of etoposide, and 3',4',5'-tridemethoxy (-) podophyllotoxin, the E-ring deoxygenated analogue of (-) podophyllotoxin; substituted podophyllotoxin aglycones are the C4 -C-podophyllotoxin aglycones *i.e.* 4 $\beta$ -alkyl, 4 $\beta$ -aminoalkyl and 4 $\beta$ -aminoalkyl derivatives of 4'-O-demethyl-4-desoxypodophyllotoxin, 1- $\beta$ -alkyl derivatives of podophyllotoxin, 4- $\beta$ -aminoalkyl-4-O-demethyl-4-desoxypodophyllotoxin (TOP-53); C4-O-podophyllotoxin aglycones include 4'-demethylpodophyllotoxin-lexitropsin conjugates, ester derivatives of the C4 hydroxyl group of 4'-demethylpodophyllotoxin, thymidine derivatives of podophyllotoxin; C4-N-podophyllotoxin aglycones include 4-hydroxylated and halogenated anilinderivatives of epipodophyllotoxin with substitution on the  $\beta$ -anilino moiety with CN, COOCH<sub>3</sub>, COOC<sub>2</sub>H<sub>5</sub>OH and COOCH<sub>3</sub>, OCH<sub>3</sub>, COCH<sub>3</sub>, CH<sub>2</sub>OH, OCH<sub>2</sub>O, OCH<sub>2</sub>CH<sub>2</sub>O, phenoxy, morpholino, NO<sub>2</sub>, either at the para and/or the meta position, 4'-demethylepipodophyllotoxin, 2'-chloro derivatives of etoposide and 4 $\beta$ -(arylamino)-4'-O-demethylpodophyllotoxin, 6,7-O,O-demethylene-4'-O-demethyl 4 $\beta$ -(substituted anilino)-4-deoxy podophyllotoxins, 6,7-O,O-demethylene-6,7-O,O-dimethyl-4'-O-demethyl-4 $\beta$ -(substituted anilino)-4-desoxypodophyllotoxins and their 4'-O-methyl analogues. Are also included 4-azido, 4-amino, amido and 4-alkoxy derivatives of podophyllotoxin and 4'-demethylepipodophyllotoxin and also ortho-quinone analogues of podophyllotoxin possessing various C-4 $\beta$ -anilino moieties, and also 4 $\beta$ -arylamino derivatives of 4'-O-demethylpodophyllotoxin and also 4'-O-demethyl-4-desoxypodophyllotoxin and 4 $\beta$ -benzoyl derivatives of 4'-O-demethylpodophyllotoxin; C4-S-podophyllotoxin aglycones are the 4'-O-demethylepipodophyllotoxin derivatives possessing various 4 $\beta$ -N-, 4 $\beta$ -O- or 4 $\beta$ -S-aromatic rings; the podophyllotoxin derivatives with one of the hydroxyl groups in the glycosidic moiety substituted by an alkylamino group; the 2-azapodophyllotoxin analogues, the 4-desoxy-2-azapodophyllotoxins, the benzoquin-olizidine analogues of podophyllotoxin, and azatoxin, which is an analogue hybrid between VP-16 aglycon and ellipticin, and its derivatives.

4. The composition of claim 1 wherein the podophyllotoxin is etoposide.
5. The composition of claim 1 wherein the surfactant is tocoferol.

6. The composition of claim 5 wherein the tocoferol is covalently linked to a water-soluble polymer.

7. The composition of claim 6 wherein the water-soluble polymer is poly-oxyethylene, poly-oxyethylene-poly-oxypropylene copolymers polyacrylamides, polyglycerols, polyvinylalcohols, polyvinylpyrrolidones, polyvinylpyridine N-oxides, copolymers of vinylpyridine N-oxide and vinylpyridine, polyoxazolines, polyacroylmorpholines or derivatives thereof.

8. The composition of claim 6 wherein the water-soluble polymer is a polypeptide or derivative thereof.

10 9. The composition of claim 6 wherein the water-soluble polymer further comprises a hydrophobic group other than tocoferol.

10. The composition of claim 1 wherein the surfactant is d- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate (TPGS) or a derivative thereof.

15 11. The composition of claim 10 wherein the TPGS is present at a concentration from about 0.02 wt % to about 20 wt %.

12. The composition of claim 10 wherein the TPGS is present at a concentration from about 0.02 wt % to about 10 wt %.

13. The composition of claim 10 wherein the TPGS is present at a concentration from about 4 wt % to about 10 wt %.

20 14. The composition of claim 1 further comprising a targeting molecule.

15. The composition of claim 14 wherein the targeting molecule comprises a targeting moiety and a lipophilic moiety.

16. The composition of claim 15 wherein the targeting moiety is an antibody, hormone, carbohydrate, drug, cytokine or interleukin.

25 17. The composition of claim 15 wherein the targeting moiety is a peptide.

18. A method of treating an animal comprising administering to the animal a composition comprising:

- (a) a podophyllotoxin, an analog thereof or a derivative thereof; and
- (b) a surfactant;

5 wherein the composition forms a micelle.

19. The method of claim 18 wherein the surfactant is TPGS or a derivative thereof.

20. A method of delivering a podophyllotoxin, an analog thereof or a derivative thereof to a cell comprising administering to the cell a composition comprising:

- (a) a podophyllotoxin, an analog thereof or a derivative thereof; and
- (b) a surfactant;

10 wherein the composition forms a micelle.

21. A method of inhibiting cancer comprising administering to an animal having cancer a composition comprising:

- (a) a podophyllotoxin, an analog thereof or a derivative thereof; and
- (b) a surfactant;

15 ~~wherein the composition forms a micelle.~~